II. AMENDMENTS TO THE CLAIMS:

1. (Currently Amended) Nitrooxyderivatives or salts thereof of ~~having the following general~~ formula (I)

~~$R-NR_{1c}(K)_{k0}-(B)_{b0}-(C)_{b0}-NO_2$ (I)~~

$R-NR_{1c}-(C)-NO_2$ (I)

~~wherein c0 is 0 or 1;~~

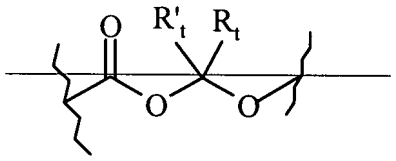
~~b0 is 0 or 1, with the proviso that c0 and b0 can not be simultaneously 0;~~

~~k0 is 0 or 1;~~

~~R is the radical of an analgesic drug for chronic pain;~~

R_{1c} [[, being]] is H ~~or straight or branched alkyl with from 1 to 5 carbon atoms~~;

~~K is (CO) or the bivalent radical (1C) having the following formula:~~



(1-C)

~~wherein the carbonyl group is bound to T_1; R_t and R'_t, same or different, are H, C_1-C_{10}-alkyl, phenyl or benzyl, $-COOR_y$, in which R_y = H, C_1-C_{10}-alkyl, phenyl, benzyl;~~

~~$B = -T_B-X_2-T_{B1}$- wherein~~

~~T_B = (CO) or X, in which X = O, S, NH;~~

~~with the proviso that:~~

~~when b0 = 1 and k0 = 0, then T_B = (CO);~~

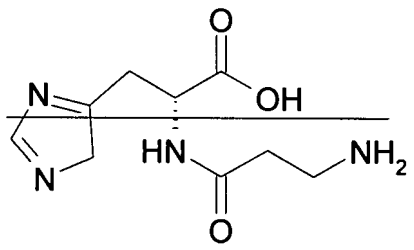
~~when b0 = 1 and k0 = 1, being K = (CO), then T_B = X as defined above;~~

~~T_{BI} = (CO) or (X), wherein X is as defined above;~~

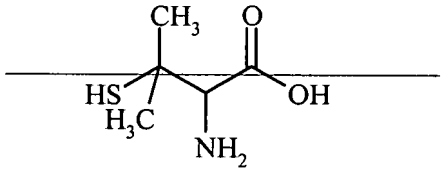
~~when c0 = 0, then T_{BI} = -0-;~~

~~X_2 is such a bivalent bridging group such as the corresponding precursor of B, having the formula Z-T_B-X_2-T_{BI}-Z' in which Z, Z' are independently H or OH, is selected from the following compounds:~~

~~Aminoacids: L-carnosine (CI), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII):~~

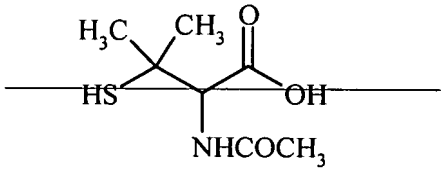


,

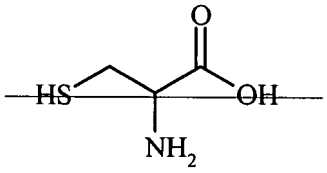


,

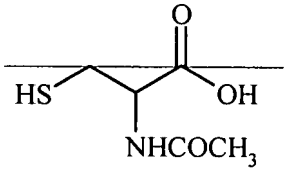
~~(CI)~~ ~~(CV)~~



,

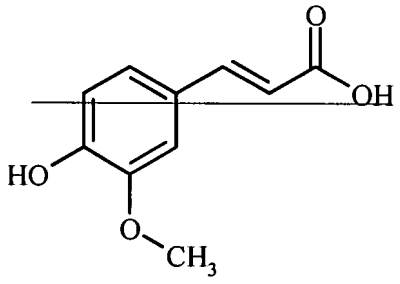


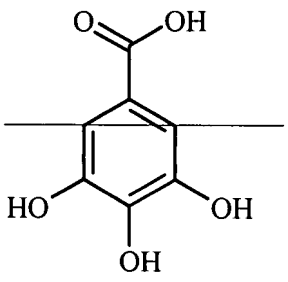
,

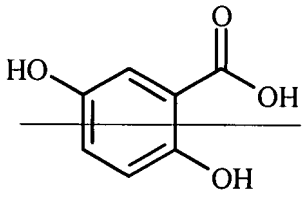


~~(CVI)~~ ~~(CVII)~~ ~~(CVIII)~~

~~Hydroxyacids: gallic acid (DI), ferulic acid (DII), gentisic acid (DIII), caffeic acid (DV), hydro caffeic acid (DVI), p-coumaric acid (DVII), vanillic acid (DVIII), syringic acid (DXI):~~

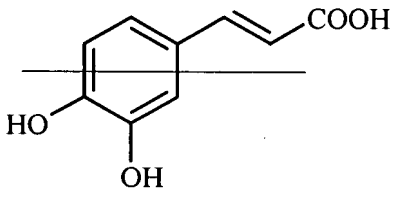


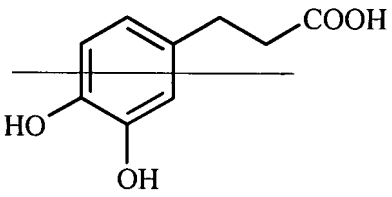
,


,


,

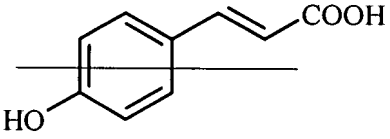
~~(DII)~~ ~~(DI)~~ ~~(DIII)~~

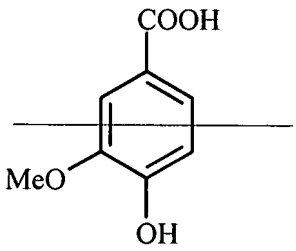


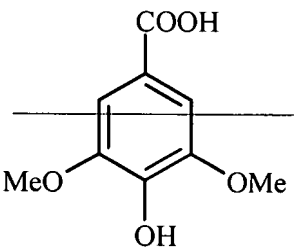
,


,

~~(DV)~~ ~~(DVI)~~



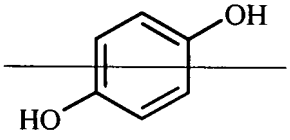
,


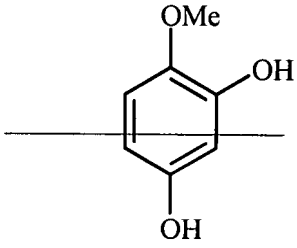
,


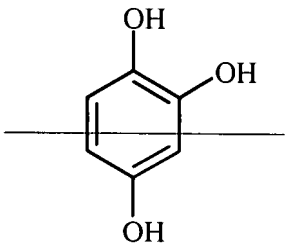
;

~~(DVII)~~ ~~(DVIII)~~ ~~(DXI)~~

~~aromatic polyalcohols: hydroquinone (EVIII), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), conyferyl alcohol (EXXXII), 4-hydroxyphenetyl alcohol (EXXXIII), p-coumaric alcohol (EXXXIV):~~

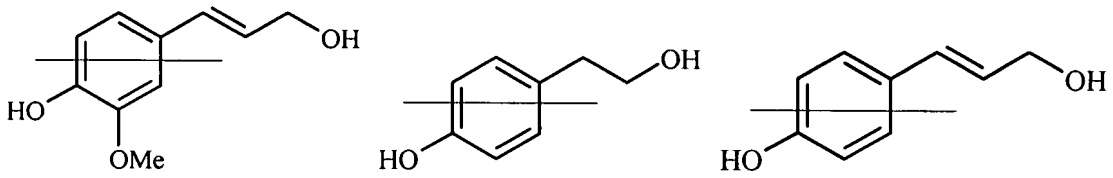


,


,


,

~~(EVIII)~~ ~~(EXI)~~ ~~(EXII)~~



~~(EXXXII)~~ ~~(EXXXII)~~ ~~(EXXXIV);~~

C = bivalent radical ~~having the~~ of formula $-T_c-Y$

wherein

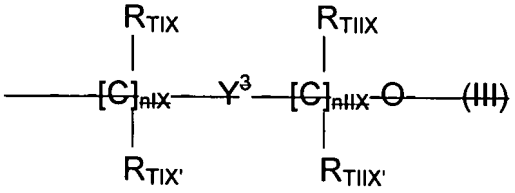
T_c = (CO) ~~or X being as defined above~~;

~~with the proviso that when b0 =0 and k0 = 1:~~

~~T_c = (CO) when K = (1C),~~

~~T_c = X as defined above when K = (CO);~~ and

Y is ~~has one of the following meanings:~~



~~wherein:~~

~~nIX is an integer of from 0 to 5;~~

~~nIIX is an integer of from 1 to 5;~~

~~R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$, the same or different, are H or straight or branched C_1-C_4-alkyl;~~

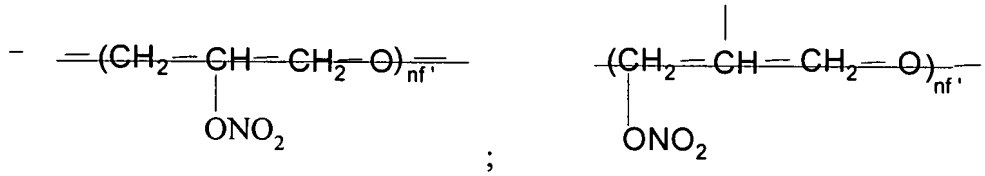
Application Serial No. 10/537,439
Attorney-Docket No. 026220-00066

~~Y^3 is a saturated, unsaturated or aromatic heterocyclic ring with 5 or 6 atoms, containing one to three heteroatoms, said heteroatoms being the same or different and selected from nitrogen, oxygen or sulphur;~~

~~or Y may be:~~

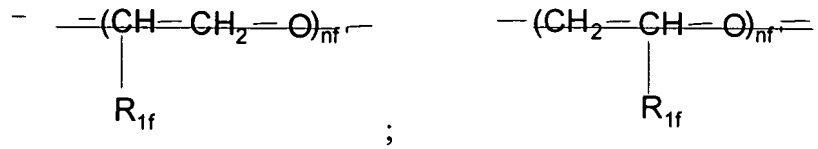
an alkylenoxy group -R'O- in which R' is straight or branched C_1-C_{20} , [[or]] a cycloalkylene with from 5 to 7 carbon atoms, or ~~, and wherein in cycloalkylene ring one or more carbon atoms can be replaced by heteroatoms and the ring may present side chains of R' type, R' being as defined above~~;

~~or one of the following groups:~~



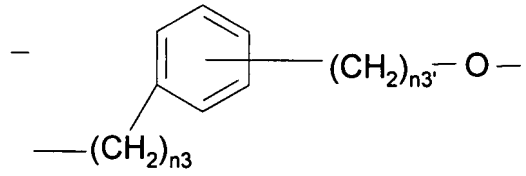
;

~~wherein nf' is an integer from 1 to 6;~~

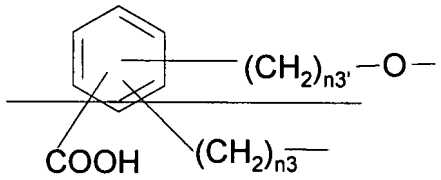


;

~~wherein R_{1f} = H, CH_3 and nf' is an integer from 1 to 6;~~

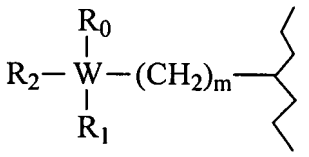


wherein n3 is an integer from 0 to 5 and n3' is an integer from 1 to 3; ~~or~~



~~in which n3 and n3' have the meaning mentioned above;~~

R is the radical of an analgesic drug ~~having~~ of formula (II):



(II)

wherein:

W is a carbon ~~or nitrogen~~ atom;

m is 1 ~~an integer of from 0 to 2~~;

R_0 = [[H,]] -$(CH_2)_n$-$COOR_y$, wherein R_y = H, C_1-C_{10}-alkyl, phenyl, or benzyl ~~being as defined above~~;

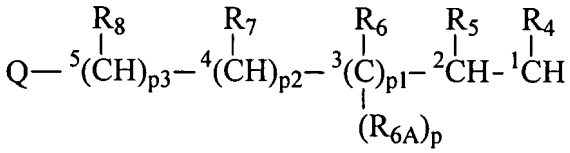
n is an integer of from 0 to 2;

R_1 = H; ~~when W = N, R_1 is the electronic doublet on nitrogen atom (free valence);~~

R_2 is selected from the following groups:

- phenyl, optionally substituted with a halogen atom or with a group selected from -OCH_3, -CF_3, nitro;
- mono or dihydroxy-substituted benzyl, preferably 3,4-dihydroxybenzyl;
- amidino group: $H_2N(C=NH)$-;

- a radical of formula (IIA), wherein optionally an ethylenic unsaturation may be present between the carbon atoms in position 1 and 2, or 3 and 4 or 4 and 5:



(IIA)

wherein:

p, p_1, p_2 are integers, same or different, and are 0 or 1;

p_3 in an integer of from 0 to 10;

R_4 is hydrogen, straight or branched C_1-C_6-alkyl, free valence;

R_5 may have the following meanings:

- hydrogen,
- straight or branched C_1-C_6-alkyl,
- C_3-C_6-cycloalkyl, or
- OR_A, R_A having the following meanings:
  - straight or branched C_1-C_6-alkyl, optionally substituted with one or more halogen atoms, preferably F,
  - phenyl optionally substituted with a halogen atom or with one of the following groups: $-OCH_3$, $-CF_3$, nitro;

R_6, R_{6A}, R_7, R_8, the same or different, are H, methyl or free valence, with the proviso that when an ethylenic unsaturation is present between C_1 and C_2 in radical of formula (IIA), R_4 and R_5 are free valences able to form the double bond between C_1 and C_2; if the unsaturation is between C_3 and C_4, R_6 and R_7 are free valence able to form the double bond between C_3 and C_4; is the unsaturation is between C_4 and C_5, R_7 and R_8 are free valence able to form the double bond between C_4 and C_5;

Q is H, OH, OR_B, R_B being benzyl, straight or branched C_1-C_6-alkyl, optionally substituted with one or more halogen atoms, preferably F, phenyl optionally substituted with a halogen atom or with one of the following groups: $-OCH_3$, $-CF_3$, nitro; or

Q may have one of the following meanings:

- straight or branched C_1-C_6-alkyl,
- C_3-C_6-cycloalkyl,
- guanidino ($H_2NC(=NH)NH-$), or
- thioguanidino ($H_2NC(=S)NH-$) [[.]] ,

in formula (II) R_2 with R_1 and with W = C form together a C_4-C_{10} saturated or unsaturated ring.

2. (Canceled)

3. (Currently Amended) Compounds according to claim 1, wherein ~~characterized in that~~ in formula (I):

~~c0 is l;~~

~~b0 is 0 or 1;~~

~~k0 is 0 or 1;~~

~~R_{1c}, =H;~~

~~K is (CO) or the bivalent radical (1C) as defined in claim 1;~~

~~B = T_B-X_2-T_{Bl} wherein~~

~~T_B = (CO) or X, in which X = O, S, NH;~~

~~with the proviso that:~~

~~when b0 = 1 and k0 = 0, then T_B = (CO);~~

~~when b0 = 1 and k0 = l, being K = (CO), then T_B = X as defined above;~~

~~T_{Bl} = (CO) or (X), wherein X is as defined above;~~

~~when c0 = 0, then T_{Bl} = O ;~~

~~the precursor of B is N-acetylcysteine or ferulic acid;~~

~~C = bivalent radical having the formula -T_c-Y-~~

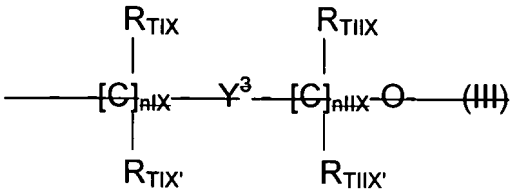
~~wherein~~

~~T_c = (CO) or X being as defined above~~;

~~with the proviso that when b0 =0 and k0 = 1:~~

- ~~T_c = (CO) when K = (1C),~~
- ~~T_c = X as defined above when K = (CO);~~ and

Y is ~~has one of the following meanings~~:

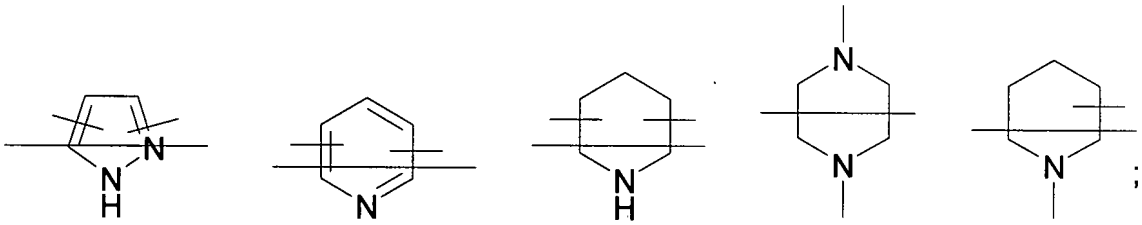


wherein:

nIX and nIIX are 1;

R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$ are H;

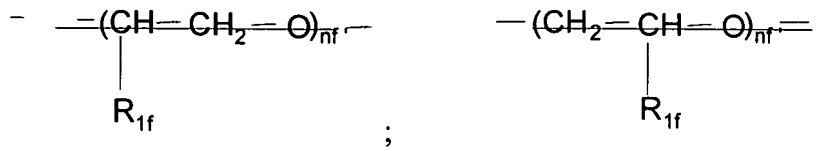
Y^3 is selected from the following bivalent radicals:



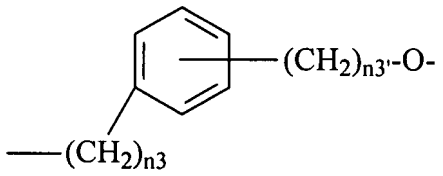
(Y1) (Y12) (Y13) (Y16) (Y19)

or Y may be:

an alkylenoxy group -R'O- in which R' is straight or branched C_2-C_6 alkyl; or

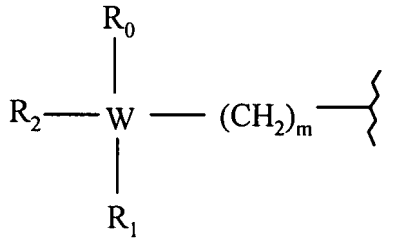


wherein Rif= H, CH_3 and nfl is an integer from 1 to 4;

– 

wherein n3 is an integer from 0 to 3 and n3' is an integer from 1 to 3;

R is the radical of an analgesic drug [[having]] <u>of</u> formula (II):



(II)

wherein:

W is a carbon atom;

m is [[0 or]] 1;

R_0 = [[H or]] <u>$-(CH_2)_n-COOH$</u> ~~$-(CH_2)_n-COOH$~~, wherein n is an integer of from 0 to 2;

R_1 = H;

R_2 is selected from the following groups:

- 3,4-dihydroxybenzyl; or
- a radical of formula (IIA) as defined in claim 1, wherein:

p and p_1 are ~~are~~ 0 or 1;

p_2 and p_3 are 0;

R_4 and R_5 are hydrogen, straight or branched C_1-C_6-alkyl or free valence;

R_6 and R_{6A} are H;

with the proviso that when an ethylenic unsaturation is present between C_1 and C_2 in radical of formula (IIA), R_4 and R_5 are free valences able to form the double bond between C_1 and C_2;

Q is H, CH_3 or

- guanidino ($H_2NC(=NH)NH$-), or
- thioguanidino ($H_2NC(=S)NH$-);

in formula (II) R_2 with R_1 and with W form together a C_6 saturated ring.

4. (Currently Amended) Compounds according to claim 1, wherein when in formula (II) W = C, m = 1 and $R_0 = -(CH_2)_n-COOR_y$, wherein n = 1 and R_y = H; R_2 and R_1 with W as defined above form the cyclohexane ring; the drug precursor of R having the formula R-NH_2 is known as gabapentin;

~~when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = 1, p_2 = p_3 = 0, R_4 = R_5 = R_6 = R_{6A} = H, Q = H; the drug precursor of R having the formula R-NH_2 is known as norvaline;~~

~~when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = 1, p_2 = p_3 = 0, R_4 = R_5 = R_6 = R_{6A} = H, Q is the guanidino group; the drug precursor of R having the formula R-NH_2 is known as arginine;~~

~~when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = 1, p_2 = p_3 = 0, R_4 = R_5 = R_6 = R_{6A} =~~

~~H, Q is the thioguanidino group; the drug precursor of R having the formula R-NH_2 is known as thiocitrulline;~~

when in formula (II) W = C, m = 1 and R_0 if defined as for gabapentin with n = 1; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = p_2 = p_3 = 0, R_4 = H, R_5 = Q = CH_3; the drug precursor of R having the formula R -NH_2 is known as pregabalin;

when in formula (II) W = C and has (S) configuration, m = 1 and R_0 if defined as for gabapentin with n = 1; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = p_2 = p_3 = 0, R_4 = H, R_5 = Q = CH_3; the drug precursor of R having the formula R-NH_2 is known as (S)3-isobutilGABA;

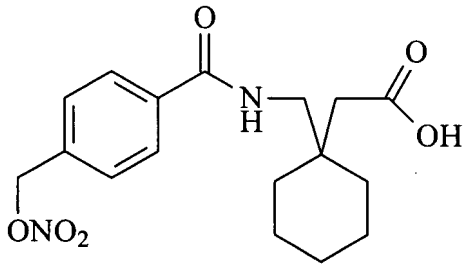
~~when in formula (II) W = C and has (S), m = 0; R_0 = R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = 1, p_2 = p_3 = 0, R_4 = R_5 = R_6 = R_{6A} = H, Q is the guanidino group; the drug precursor of R having the formula R-NH_2 is known as agmatine;~~

~~when in formula (II) W = C, m = 0; R_0 if defined as for gabapentin with n = 2; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = p_2 = p_3 = 0, R_4 and R_5 are free valences and between C_1 and C_2 there is an ethylenic unsaturation, Q = H; the drug precursor of R having the formula R-NH_2 is known as vigabatrin;~~

~~when in formula (II) W = C, m = 0; R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the 3,4-dihydroxybenzyl radical; the drug precursor of R having the formula R-NH_2 is known as 2-amino-3-(3,4-dihydroxyphenylpropanoic acid (dopa)~~.

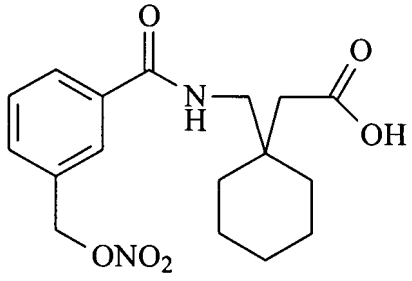
5. (Canceled)

6. (Currently Amended) Compounds according to claim 1 selected from: 1-[4-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVA),



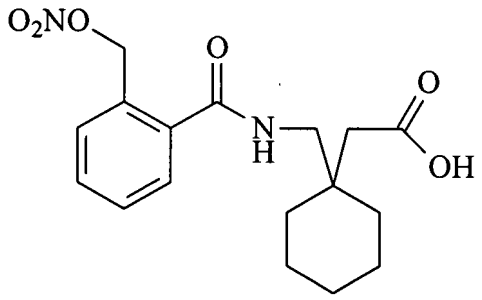
(XVA)

1-[3-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVIA),



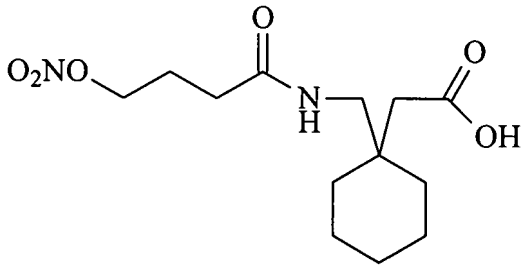
(XVIA)

1-[2-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVIIA),



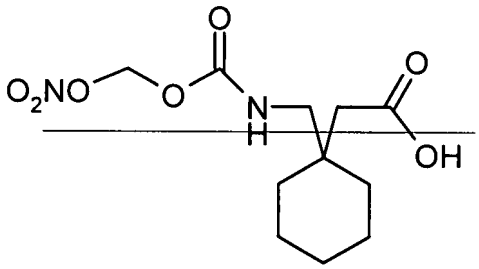
(XVIIA)

1-(4-nitrooxybutanoylaminomethyl)-cyclohexaneacetic acid (XVIIIA),



(XVIIIA)

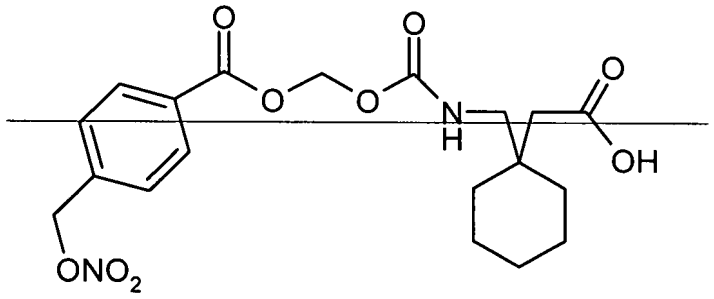
~~1-(nitrooxymethoxycarbonylaminomethyl)-cyclohexaneacetic acid (XIXA),~~



~~(XIXA)~~

~~1-{[4-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid~~

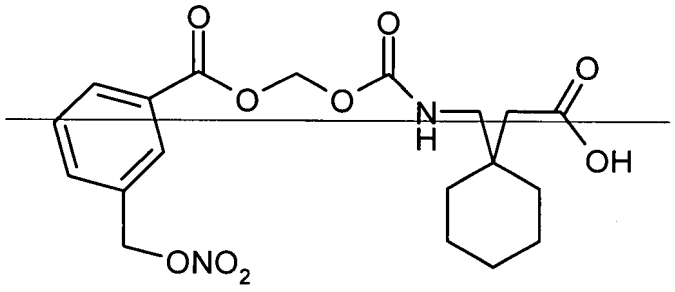
~~(XXA),~~



~~(XXA)~~

~~1-{[3-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid~~

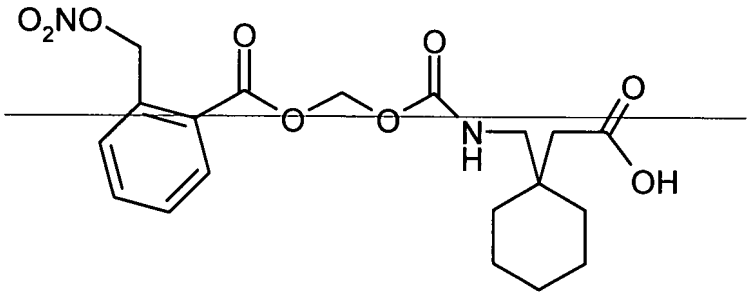
~~(XXIA),~~



~~(XXIA)~~

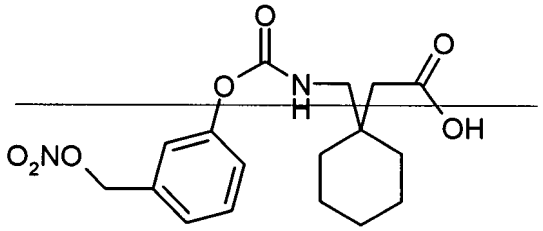
~~1-{[2-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid~~

~~(XXIIA),~~



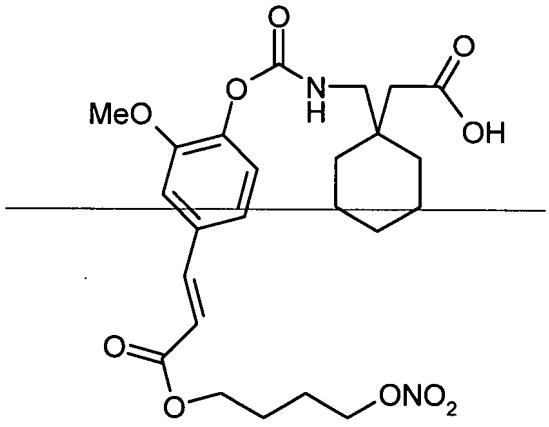
~~(XXIIA)~~

~~1-[3-(nitrooxymethyl)phenoxycarbonylaminomethyl]-cyclohexaneacetic acid (XXIIIA),~~



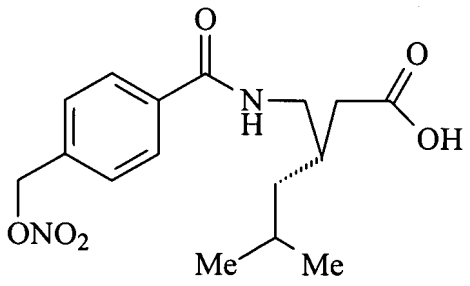
~~(XXIIIA)~~

~~{2-methoxy-4-[(1E)-3-[4-(nitrooxybutoxy)-3-oxa-1-propenylphenoxy]-carbonylamino-methyl}-cyclohexaneacetic acid (XXIVA),~~



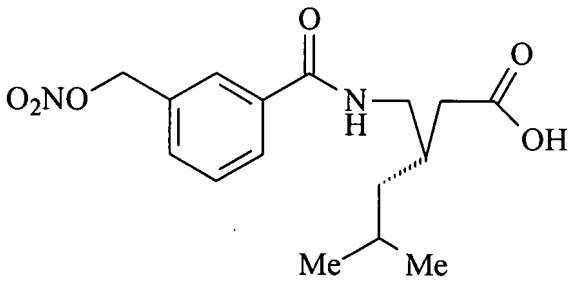
~~(XXIVA)~~

3-(S)-[4- (nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVA),



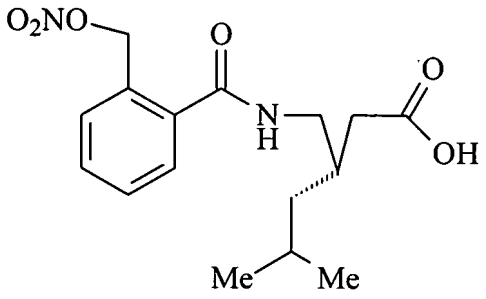
(XXVA)

3-(S)-[3-(nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVIA),



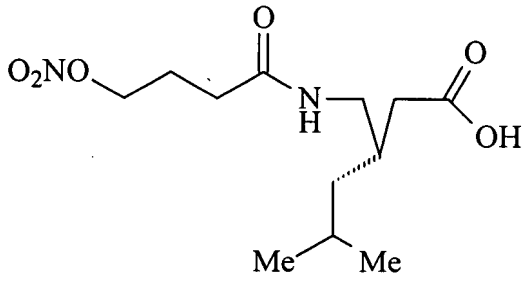
(XXVIA)

3(S)-[2-(nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVIIA),



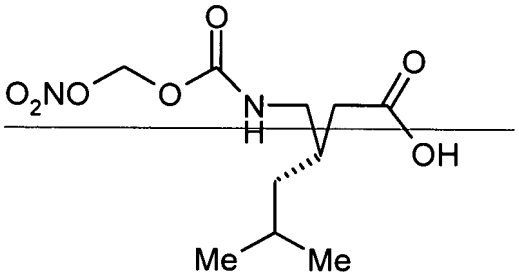
(XXVIIA)

3(S)-[4-(nitrooxybutanoyl)aminomethyl]-5-methyl-hexanoic acid (XXVIIIA),



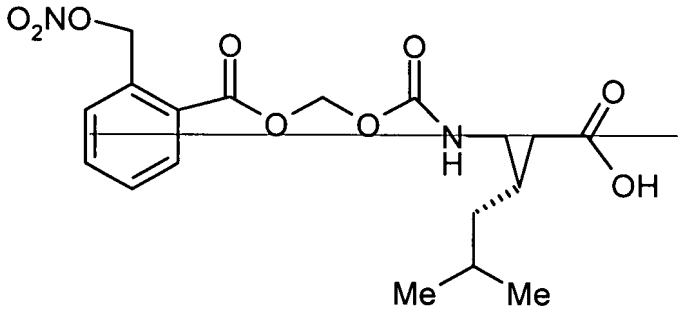
(XXVIIIA)

~~(S)-[4-(nitrooxymethoxycarbonyl)aminomethyl]-5-methyl-hexanoic acid (XXIXA),~~



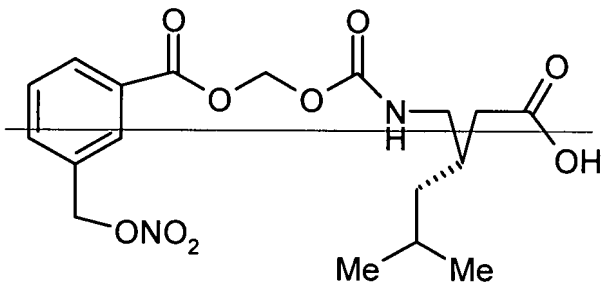
~~(XXIXA)~~

~~3(S)-{[2-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXA),~~



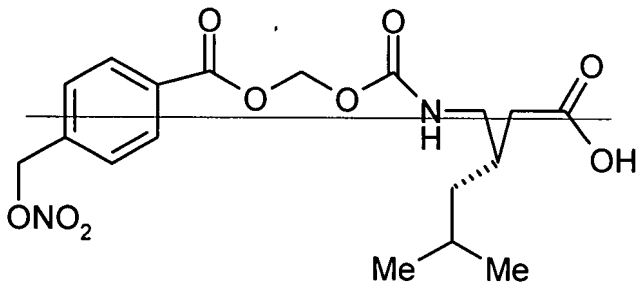
~~(XXXA)~~

~~3(S)-{[3-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXIA),~~



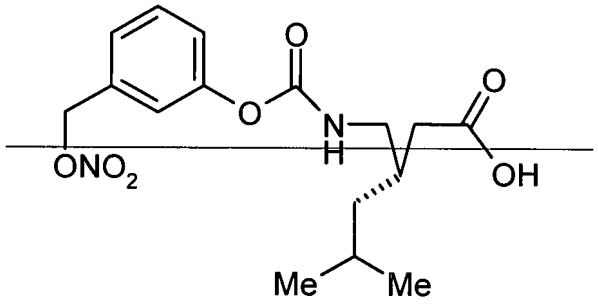
~~(XXXIA)~~

~~3(S)-[4-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXIIA),~~



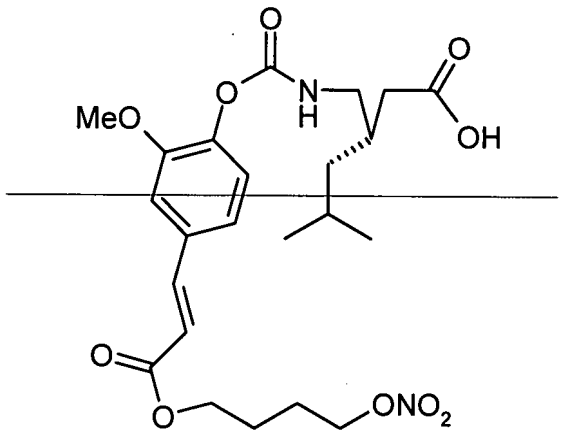
~~(XXXIIA)~~

~~3(S)-[(3-nitrooxymethyl)phenoxycarbonylaminomethyl]-5-methyl-hexanoic acid (XXXIIIA),~~



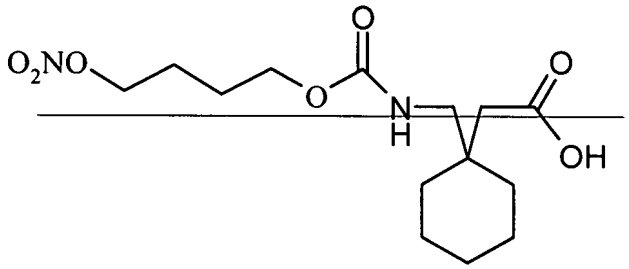
~~(XXXIIIA)~~

~~3(S)-[2-methoxy-4-[(1E)-3-[4-(nitrooxybutoxy]-3-oxa-1-propenylphenoxy]carbonyl-aminomethyl]-5-methyl-hexanoic acid (XXXIVA),~~



~~(XXXIVA)~~

~~1-[4-(nitrooxybutyloxycarbonyl)aminomethyl]-cyclohexaneacetic acid (XXXVA),~~



~~(XXXVA)~~

7. (Previously Presented) Compounds according to claim 1, in combination with NO-donor compounds.

8. (Original) Compounds according to claim 7, wherein the NO-donors contain in the molecule radicals of the following drugs: aspirin, salicylic acid, ibuprofen, paracetamol, naproxen, diclofenac and flurbiprofen.

9. (Previously Presented) Pharmaceutical compositions comprising compounds according to claim 1 as active ingredients.

10. (Previously Presented) Compounds according to claim 1 to be employed as a drug.

11. (Withdrawn and Currently Amended) ~~Use of~~ A method of treatment of chronic pain comprising administering an effective amount of the compounds according to claim 1 ~~for preparing drugs for chronic pain~~.

12. (Withdrawn and Currently Amended) ~~Use of the compounds~~ The method according to claim 11, wherein the chronic pain is neurophatic pain.